REMARKS

Applicant acknowledges receipt of the Restriction Requirement mailed July 28, 2008. With the present Response, Applicant cancels claims 1-21, 27, 29, 46-47, and 53-60. Applicant also amends claims 23, 26, 28, 30, 32, 33 and 38. Applicant also presents new claims 61-70. Support for the new claims is found in the currently canceled claims as well as throughout the specification. No new matter is presented. Reconsideration is earnestly solicited.

In response to the restriction requirement, Applicant elects, with traverse, Group III (Claims 30, 31 and 33-37) drawn to methods of increasing the level of splicing at a specific splice site. Applicant presents currently amended claims which include the claims of Group II, which have been restricted to splicing, as well as Groups IV and V which are also limited to splicing. Claim 23, as amended, is directed to a method of recruiting an RNA splicing factor to a target RNA species by providing a nucleic acid molecule having two functional domains as defined. As explained below, the technical features claimed provide a single general inventive concept required under PCT Rule 13 and, thus, restriction is improper.

Independent Claim 23 (Group II, as amended) encompasses each of the remaining claims and groups of inventions making restriction improper as per PCT Rule 13. The claims of Group III (increasing the level of splicing), Group IV (increasing the level of incorporation of a specific exon) and Group VI (treating a condition characterised by defective splicing) all require the use of a molecule as defined in Claim 23 and act by recruiting an RNA splicing factor to a target RNA species as specified in Claim 23. Moreover, the inventions of Groups III and IV are provide a single general inventive concept because Group IV belongs to Group III. The reason for this single general inventive concept is that an exon is bounded by splice sites (at least one, by definition). Methods of stimulating inclusion of an exon have to stimulate splicing at one or both (usually there are two) of the flanking splice sites. All exons have one or two splice sites, and all splice sites bound an exon. However, since there can be alternative splice sites around an exon and it is possible to stimulate use of only one, selectively, then it is appropriate to have an additional complementary claim that refers to selecting a specific exon. Group VI is also in the single general inventive concept because the treatment requires the same compounds and acts in the same way.

Applicant further submits that the Examiner's rejection is improper and should be

withdrawn because, firstly, the guidelines referred to by the Examiner are only applicable in the context of claims to chemical compounds *per se*, and not to methods of using such compounds. Thus, *a priori*, the reasons for lack of unity provided by the Examiner cannot be applicable to any of the methods that are presently claimed. Indeed, it is commonly accepted patent practice that a novel and inventive use can provide unity to an otherwise diverse group of compounds. Accordingly, the claimed use of the compounds, "recruiting an RNA splicing factor to a target RNA species", which itself is sufficient to provide a single general inventive concept, should be taken into consideration.

Secondly, the criteria used by the examiner were designed for chemical compounds and as such are not appropriate in the context of biological molecules which are typically much larger, and are routinely defined functionally rather than structurally. This can be shown, for example, by reference to antibodies. Various different antibodies that bind to separate and distinct epitopes of a single molecule possess unity of invention despite the fact that the CDR regions of the antibodies do not share a common sequence. Indeed, this is also true even if the backbone regions of the various antibodies are also distinct. Nevertheless, by virtue of their shared function of binding to a single specific molecule, they are considered to be the same invention. When assessing unity of invention under PCT Rule 13, it would be more appropriate to consider the claims as a whole. The nucleic acid molecules, as defined in Claim 23, each have the same properties and function. That is, the first domain is a targeting domain that targets the molecule to a desired RNA species, and the second domain acts to recruit an RNA splicing factor to the target RNA species. Accordingly, the claimed molecules do possess common structural elements as well as common properties that are directly related to the claimed use of the molecules.

Lastly, Applicant notes that even if the examiner was correct that the claims lack unity for the reasons given, this would not result in the groups of inventions delineated by the Examiner. None of the reasons given by the examiner explains the distinction between Groups III, IV and VI (and II in part) which all relate to enhancing splicing. As explained above, under PCT Rule 13, this is sufficient to provide unity of invention – and this was accepted by the International examiner. Thus, despite the reference to the PCT guidelines, the Examiner appears to have applied US restriction standards, and not PCT standards for assessing unity of invention.

With regards to the requirement to elect a single target gene, Applicant elects SMN2 as in

Example 1 of the present application. Thus, the first domain of the molecule is one that will bind to SMN2. For the second domain, Applicant elects that it binds to the RNA splicing factor SF2/ASF. For an RNA process, Applicant elects splicing and, for a therapeutic activity, Applicant elects the treatment of spinal muscular atrophy (SMA).

CONCLUSION

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated, since this should expedite the prosecution of the application for all concerned.

A fee for a one-month extension of time is submitted contemporaneously herewith. The Commissioner is further authorized to charge any deficiency in fees or credit any overpayments to Deposit Account No. 09-0528 (Docket # E072 1050.1).

Respectfully submitted,

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